Craniocervical Paraganglioma With Numerous Pulmonary Metastases

—Case Report—

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Abstract

A 28-year-old man presented with a rare craniocervical paraganglioma with multiple pulmonary metastases manifesting as hearing disturbance, hoarseness, and dysphagia in February 2003. Magnetic resonance imaging depicted a large jugular foramen tumor extending to the deep cervical region. Chest computed tomography revealed numerous small pulmonary nodules. The jugular tumor was totally resected immediately after preoperative embolization. Histological examination revealed paraganglioma. Localized irradiation (54 Gy) and two courses of combination chemotherapy consisting of paclitaxel (80 mg/m²) and gemcitabine (1000 mg/m²) were given. The patient remained well during follow up for 48 months and the number of pulmonary metastases did not increase. Local control of primary craniocervical paraganglioma by palliative surgical resection may be effective for control of metastatic lesions.

Key words: chemotherapy, paraganglioma, palliative surgery, pulmonary metastasis

Introduction

Jugular paraganglioma, also called glomus jugulare tumor or chemodectoma, is a neuroendocrine tumor derived from the paraganglia of the parasympathetic nervous system in the jugular bulb. Jugular paraganglioma was first reported in 1945,¹ and is the commonest benign tumor of the neck. Distant metastases from the jugular paraganglioma are very rare with a reported incidence of 1–4%,³ which is probably overestimated due to preferential reporting of cases with metastases and the occurrence of multicentric paraganglioma.

Malignant behavior occurs in approximately 1% to 4% of jugular paragangliomas and 16% of vagal paragangliomas. The major criterion for malignancy is metastasis to the cervical lymph nodes or distant sites such as the lung, bone, breast, and liver,⁴ and is more common in the sporadic type of paraganglioma unrelated to tumor size. Histological features including nuclear pleomorphism, atypia, and mitotic activity are not considered as to define signs of malignancy in paraganglioma. The most common site of metastasis from jugular paraganglioma is the lung followed by the cervical lymph node.² The management of paraganglioma with distant metastases remains controversial.

We treated a patient with jugular paraganglioma who presented with multiple pulmonary metastases that did not change over a 4-year period after palliative resection of the primary tumor.

Case Report

A 28-year-old man was referred to Hokkaido University Hospital with a 12-month history of right pulsatile tinnitus and hearing loss in February 2003. Neurological examination found hoarseness and dysphagia caused by right vagal and glossopharyngeal nerve pareses. Physical examination revealed no abnormality including body temperature, pulse rate, and blood pressure. Serum levels of catecholamine
Fig. 1 Coronal (A, B) and axial (C, D) $T_1$-weighted magnetic resonance images with gadolinium on admission demonstrating an enhanced mass in the right parapharyngeal region.

Fig. 2 Pre-embolization digital subtraction angiograms demonstrating multicentric paragangliomas, mainly fed by the occipital artery (left, arrowheads) and the ascending pharyngeal artery (right, arrowheads), which was remarkably shifted anteriorly by the tumor.

Fig. 3 Chest computed tomography scans demonstrating multiple small parenchymal nodules.

Magnetic resonance (MR) imaging with gadolinium showed a large jugular foramen tumor on the right extending to the cerebellopontine angle, the parapharyngeal space, and the carotid space at the C3 level (Fig. 1). MR imaging also showed multiple flow voids surrounding the tumor and intratumoral hematomas. Digital subtraction angiography demonstrated that the tumor consisted of two components, a jugular tumor and a vagal tumor supplied from the vertebral artery and the external carotid artery (Fig. 2). Chest radiography and computed tomography demonstrated multiple small nodular lesions, varying in size from several millimeters to 10 mm, scattered throughout the bilateral pulmonary fields (Fig. 3). Multicentric craniocervical paraganglioma with multiple pulmonary metastases was highly suspected based on these findings. Resection of the primary tumor as palliative treatment for control of the tumor was planned considering the size of the tumor and the patient’s age. Two days prior to the surgical removal, the tumor was embolized using polyvinyl alcohol to reduce intraoperative bleeding.

Surgical resection was performed through a longitudinal retroauricular incision along the anterior border of the sternocleidomastoid muscle. Proximal control of the external carotid artery and the vertebral artery were carefully obtained to prevent injury to the adjacent cranial nerves. All feeding artery branches encountered were ligated or divided by bipolar cautery near to the tumor border to facilitate mobilization of the tumor and reduce blood loss. The mastoid process was removed, and the sigmoid sinus, the jugular bulb, and the facial nerve were skeletonized. After transposing the facial nerve anteriorly, the tumor in the jugular foramen and the in-
Fig. 4  Photomicrographs of the surgical specimen showing paraganglioma with Zellballen. A: Medium power view showing polygonal cells with pale cytoplasm and round nuclei with some pleomorphism, and a packeted architecture with groups of cells separated by fine fibrovascular tissue. Hematoxylin and eosin stain, × 200. B: Immunostaining using antibody to chromogranin A demonstrating positive expression within the cytoplasm of the tumor cells. × 200. C: Immunostaining using antibody to synaptophysin demonstrating positive expression within the cytoplasm of the tumor cells. × 200.

tradural space was totally removed after cutting the feeding arteries from the posterior inferior cerebellar artery. In addition, the cervical lymph nodes inferior to the tumor were excised. A spinal drainage tube was inserted within 2 weeks to prevent cerebrospinal fluid leakage.

Histological examination revealed an arrangement of indistinctive cell balls, Zellballen, positive for chromogranin A and synaptophysin characteristic of benign paraganglioma (Fig. 4). No nuclear atypia, necrosis, or anaplasia were observed. Postoperative MR imaging revealed no residual tumor in the parapharyngeal space (Fig. 5). However, some cervical lymph node metastases remained. Therefore, the primary tumor was treated with irradiation (54 Gy in 27 fractions), and then two cycles of combination chemotherapy using paclitaxel (80 mg/m²) followed by gemcitabine (1000 mg/m²), given intravenously weekly for total 4 weeks. \(^1\)

However, the pulmonary metastases did not respond to this combination chemotherapy, so he was discharged without receiving further adjuvant therapy.

At discharge, he compensated well for the ninth and tenth cranial nerve pareses, and had retained full activities of daily living without pulmonary symptoms. No local recurrence and no more pulmonary metastases were observed during the 48 months follow-up period, although some pulmonary lesions slightly increased in size without causing symptoms.

Discussion

The long-term prognosis for patients with metastases from jugular paraganglioma remains unclear.\(^5,6,11,16,19–21\) All reported cases with metastases had uncontrolled primary tumors, many with intracranial extension, so whether the primary tumor or metastases was responsible for death is unknown. Jugular paraganglioma with metastases is generally believed to be rapidly fatal, as all of three patients died within 1 year.\(^11\) On the other hand, a patient with regional metastasis had a 20-year history of the disease with no progression until the last 5 years.\(^20\) In addition, metastasis may occur years after detection of the primary lesion. Pulmonary metastasis developed 11 years later,\(^15\) and systemic metastases of paraganglioma occurred only 20 years after treatment of primary paraganglioma,\(^2\) indicating that patients with jugular paraganglioma require follow up for life to detect recurrence.

Survival of patients with paraganglioma and metastases varies from 1 to 25 years.\(^22\) Patients with metastatic paraganglioma might survive for a prolonged period without treatment.\(^6\) Therefore, the treatment method is difficult to select, because of the high risk of radical resection of primary craniocervical paraganglioma and unpredictable prognosis of the multiple pulmonary metastases. Local and regional control obtained in case of paraganglioma with pulmonary metastases resulted in remission.\(^2\)
Similarly, local control of primary paraganglioma by palliative surgical resection might have inhibited further metastases in the present case, as seen in well-differentiated thyroid cancer and renal cell carcinoma.\(^7\)\(^8\)\(^12\)\(^17\)\(^18\)

Local resection of paraganglioma in a patient with metastatic spread will remove the source of new metastases, but almost certainly will not cure the disease, and the patient may die of the metastases. Longer survival can only be achieved if improved tumor control is obtained. Resection of the primary renal cell carcinoma may induce spontaneous regression of metastases. In our case, the number of pulmonary metastases did not increase for 48 months, no additional symptom appeared, and the growth of the lesions appeared extremely slow. Resection of the primary lesion may slow the progression of pulmonary metastases, possibly involving the immune system as seen in renal cell carcinoma.\(^8\)\(^12\)\(^17\)\(^18\)

The efficacy of radiation therapy and chemotherapy in the management of paraganglioma remains unclear. Paragangliomas are known to be radioresistant, but external irradiation may occasionally suppress growth.\(^7\) Chemotherapy for paraganglioma with metastases has been reported to be basically unsuccessful.\(^10\) In our case, combination chemotherapy of paclitaxel and gemcitabine showed no obvious improvement for the pulmonary metastases. Therefore, radical resection of the primary jugular paraganglioma might be the most effective method for control of the pulmonary metastases.

References


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